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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/367,496	AGUERA ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,7,9,10,15,20-22,30 and 33-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4* is/are allowed.

6)☒ Claim(s) *1,3,6,7,9,10,15,20-22,30 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 November 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to Comply; USPTO Search Report "us-09-367-496c-7.rge".

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 6, 2005 has been entered.

1. The amendment filed September 6, 2005 is acknowledged and has been entered. Claims 14, 24, 25, and 29 have been canceled. Claims 9, 15, 20, 22, 30, and 33 have been amended. Claim 36 has been added.

2. Claims 1, 3, 4, 6, 7, 9, 10, 15, 20-22, 30, and 33-36 are pending in the application and are currently under prosecution.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The following Office action contains NEW GROUNDS of rejection.

Grounds of Objection and Rejection Withdrawn

5. Unless specifically reiterated below, Applicant's amendment filed September 6, 2005 has obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed April 6, 2005.

Allowable Subject Matter

6. The indicated allowability of claim 4 is withdrawn in view of a newly discovered reference. Rejections based on the newly cited reference follow.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 102

7. The rejection of claims 1, 9, 10, 20, 21, 30, and 36 under 35 U.S.C. 102(b) as being anticipated by Honnorat et al. (*J. Neurol. Neurosurg. Psych.* 1996; **61**: 270-278) (of record), as evidenced by Honnorat et al. (*Eur. J. Neurosci.* 1999 Dec; **11** (12): 4226-4232), is maintained.

At pages 2-5 of the amendment filed September 6, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has again argued that it is not proper to rely upon Honnorat et al. (1999) to provide evidence that Honnorat et al. (1996) anticipates the claimed invention. These arguments have been addressed in the preceding Office action and have not been found persuasive for the reasons given therein.

In addition, Applicant has argued that Honnorat et al. (1996) did not fully characterize the isolated proteins. In reply, it is irrelevant whether the prior art fully characterized the isolated proteins, as the only relevant question to ask is, does the prior art anticipate the claimed invention?

Applicant has remarked that the Examiner does not explain what factual evidence provided by Honnorat et al. (1999) shows the 66 kDa protein isolated by Honnorat et al. (1996) is the same protein as that claimed.

Is it Applicant's position that the 66 kDa protein that was isolated by Honnorat et al. (1996) is somehow different from the claimed invention? If so, how is the protein disclosed by the prior art different from that which is now claimed?

The Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed nucleic acid. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed nucleic acid molecule is different than that taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

To still further address Applicant's remark, it is noted that Applicant subsequently comments that Honnorat et al. (1999), published after the filing date of the application, describes the work of the inventors, and to a large extent shares the content of the application. It would seem therefore that Applicant, better than anyone else, should know whether the protein isolated by Honnorat et al. (1996) is the same as, or different from the claimed polypeptide.

Again, if it is Applicant's assertion that the protein isolated by Honnorat et al. (1996) is somehow different than that which is claimed, then, it suggested that Applicant remedy this issue by providing a showing of factual evidence that supports that assertion.

Finally, with regard to claim 30, Applicant has argued that Honnorat et al. (1996) does not teach a fragment of a purified ULIP polypeptide comprising the amino acid sequence of SEQ ID NO: 8. If, by these remarks, Applicant has intended to argue that Honnorat et al. does not teach a fragment of the isolated 66 kDa polypeptide, it aptly noted that claim 30 is directed to a reagent comprising a solid support (i.e., brain tissue) to which is attached (e.g., by fixation) "a peptide comprising a fragment of the polypeptide of claim 1". Because the intact 66 kDa polypeptide *comprises* a fragment of itself, claim 30 is anticipated by the prior art's disclosure of fixed specimens of human brain tissue.

8. The rejection of claims 30 and 36 under 35 U.S.C. 102(b) as being anticipated by Antoine et al. (*J. Neurol. Sci.* 1993 Jul; **117** (1-2): 215-223) (of record), as evidenced by Honnorat et al. (*Eur. J. Neurosci.* 1999 Dec; **11** (12): 4226-4232), is maintained.

At pages 5-7 of the amendment filed September 6, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that there is no indication in Antoine et al. (1993) that the serum from a patient with a paraneoplastic neurological syndrome (PNS) contains antibodies that bind a 66 kDa human protein having the amino acid sequence set forth as SEQ ID NO: 8. In reply, the claims are drawn to a reagent comprising "a solid support" and a peptide comprising a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO: 8 that binds to anti-CV2 antibodies. As such it is only relevant to ask whether the prior art teaches such a reagent; it is

not relevant to ponder whether Antoine et al. teaches the serum from a patient with a PNS contains antibodies that bind a 66 kDa human protein having the amino acid sequence set forth as SEQ ID NO: 8. As explained in the preceding Office action, given claim 31, for example, the "solid support" to which the claims are directed is reasonably interpreted as a fixed specimen of human brain tissue, and as evidenced by Honnorat et al. (1999), Antoine et al. teaches the claimed invention, since Antoine et al. teaches fixed specimens of brain tissue acquired from humans.

Furthermore, Applicant has argued that there is no evidence that a peptide comprising a fragment of a polypeptide comprising SEQ ID NO: 8 was attached to a "solid support" in the process of fixing sections of human brain. In response, it is well-understood fact that the process of "fixing" a specimen of tissue involves exposing the tissue to a "fixative". As defined, for example, by The Online Medical Dictionary (published at the Centre for Cancer Education, University of Newcastle upon Tyne), which is available on the Internet at http://cancerweb.ncl.ac.uk/omd/, "fixatives" are agents "employed in the preparation of histologic or pathologic specimens for the purpose of maintaining the existing form and structure of all of the constituent elements" (© Copyright 1997-2005 - The CancerWEB Project). Antoine et al. teaches the fixation process that was used to prepare specimens for immunocytochemical analysis; see, e.g., page 216, column 2, through page 217, column 1. In preparing specimens of human brain, Antoine et al. teaches pieces of post mortem adult brain tissue were fixed in a buffer containing 4% paraformaldehyde and 0.2% picric acid (page 217, column 1). It is understood that such fixation would be sufficient to maintain the existing form and structure of all of the constituent elements of the tissue, including, in particular, the 66 kDa protein, which, as evidenced by Honnorat et al. (1999), is present in such tissue and capable of binding to anti-CV2 antibodies.

Applicant has again argued that it is not proper to rely upon Honnorat et al. (1999) to provide evidence that the fixed brain tissue sections disclosed by the prior art do in fact comprise an attached peptide comprising a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO: 8, which binds to anti-CV2 antibodies. These arguments have been addressed in the preceding Office action and have not been found persuasive for the reasons given therein.

Claim Rejections - 35 USC § 103

9. The rejection of claims 3, 6, 7, 15, 22, and 33-35 under 35 U.S.C. 103(a) as being unpatentable over Honnorat et al. (*J. Neurol. Neurosurg. Psych.* 1996; **61**: 270-278) (of record), as evidenced by Honnorat et al. (*Eur. J. Neurosci.* 1999 Dec; **11** (12): 4226-4232), in view of US Patent No. 6,455,267 B1, is maintained.

At pages 7-14 of the amendment filed September 6, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that the Examiner has wrongly concluded that the isolated 66 kDa protein, which is disclosed by the prior art, is the same protein described in the evidentiary reference, namely Honnorat et al. (1999). In response, the Office has properly rejected the claims over the prior art, since, as evidenced by Honnorat et al., the 66 kDa polypeptide disclosed by the prior art is reasonably deemed the same as the claimed polypeptide. Is there a difference between the proteins disclosed by Honnorat et al. (1996) and Honnorat et al. (1999)? Moreover, what factual evidence of record is there that suggests the proteins are not the same? If there are any differences between the protein isolated by Honnorat et al. and the protein described by Honnorat et al., Applicant has the burden of showing those differences.

The Examiner has reasonably concluded that the isolated polypeptide disclosed by the prior art is the same as that which is claimed, since the isolated polypeptide has a molecular mass of 66 kDa, as does the claimed polypeptide comprising the amino acid sequence of SEQ ID NO: 8. The prior art teaches the isolated polypeptide binds to anti-CV2 antibodies, as does the claimed polypeptide comprising the amino acid sequence of SEQ ID NO: 8. The prior art teaches the isolated polypeptide is present in human brain, as is the claimed polypeptide comprising the amino acid sequence of SEQ ID NO: 8. This conclusion is further supported by the disclosures of the evidentiary reference, namely Honnorat et al. (1999). Honnorat et al. (1999) teaches some of the same results presented had already been reported in full detail in other publications, including, in particular, Honnorat et al. (1996); see, e.g., page 9, column 1. It is thus apparent that the studies disclosed by Honnorat et al. (1999) are extensions of those studies disclosed by Honnorat et al. (1996). Again, as noted previously, since Applicant

comments that Honnorat et al. (1999), published after the filing date of the application, describes the work of the inventors, and to a large extent shares the content of the application, it would seem that Applicant, better than anyone else, should know whether the protein isolated by Honnorat et al. (1996) is the same as, or different from the claimed polypeptide. So, if it is indeed Applicant's assertion that the protein isolated by Honnorat et al. (1996) is somehow different than that which is described by Honnorat et al. (1999) and moreover different from that which is claimed, then, it suggested again that Applicant remedy this issue by providing a showing of factual evidence that supports that assertion.

Applicant has argued that it not an inherent feature of every brain protein that appears to have a molecular mass of 66 kDa to comprise the amino acid sequence set forth as SEQ ID NO: 8. Of course, it not an inherent feature of every brain protein that appears to have a molecular mass of 66 kDa to comprise the amino acid sequence set forth as SEQ ID NO: 8. Nevertheless, as explained above, because, for example, the isolated 66 kDa polypeptide disclosed by the prior art is expressed by human brain cells and binds to anti-CV2 antibodies, the polypeptide disclosed by the prior art is reasonably deemed the same as that which is claimed. Furthermore, given the fact that the studies disclosed by Honnorat et al. (1999) are extensions of the studies disclosed by the prior art, and moreover that Honnorat et al. (1996) actually include results that were already disclosed by the prior art, it seems unreasonable that Applicant has taken the position that the isolated polypeptide disclosed by the prior art is somehow different than the protein described by Honnorat et al. (1999) without having provided any factual evidence supporting such a position.

Applicant has argued that it cannot be deduced from the disclosure of Honnorat et al. (1996) that the isolated protein comprises the amino acid sequence of SEQ ID NO: 8 and furthermore Honnorat et al. (1999) does not make possible the unambiguous identification of the isolated protein as such a protein comprising the amino acid sequence of SEQ ID NO: 8. Elsewhere, Applicant has also argued that the Examiner is only speculating that the isolated protein is the same as that which is now claimed. These arguments have been already addressed herein and in the preceding Office action and have not been found persuasive.

Applicant has again argued that it is not proper to use Honnorat et al. (1999) as an evidentiary reference. These arguments have been addressed in the preceding Office action and have not been found persuasive for the reasons given therein.

It is thus believed that Applicant's arguments have been carefully considered in their entirety, but have nonetheless not been found persuasive to overcome this or any of the above grounds of rejection that have been maintained herein.

New Grounds of Objection

Specification

10. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

11. The specification is objected to because the brief descriptions of Figures 9-12, which each consist of 4 sheets that depict different parts of the same drawing, do not indicate that there are such parts. This issue may be remedied by amending the brief descriptions of Figures 9-12 at page 18 of the specification to identify the figures as including their different parts. For example, the brief description of Figure 9 should be amended to recite, "Figure 9A-D"; and as explained below, each of the sheets depicting a part of Figure 9 should be labeled accordingly (e.g., "Fig. 9A", "Fig. 9B", "Fig. 9C", and Fig. 9D").

Drawings

12. The drawings are objected to because each of Figures 9-12 consists of 4 sheets that depict parts of the same drawing. Each sheet of any of these figures should be labeled as part of the same drawing (e.g., "A", "B", "C", and "D"). For example, the four sheets of Figure 9 should be labeled as "Fig. 9A", "Fig. 9B", "Fig. 9C", and Fig. 9D".

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the

renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

13. The drawing set forth as Figure 12 is also objected to because the figure depicts an amino acid sequence, which is incorrectly identified as SEQ ID NO: 8 in the brief description of figure at page 18.

The amino acid sequences that are depicted in Figure 12 are not listed in the Sequence Listing.

Sequences appearing in the specification and/or drawings must be identified by a sequence identifier in accordance with 37 C.F.R. 1.821(d); sequence identifiers for sequences appearing in the drawings may appear in the drawings or in the brief description of the drawings.

A replacement drawing sheet, including the correction, is required, if the drawings are objected to. See 37 CFR 1.121(d).

However, this ground of objection would be withdrawn, so that a replacement drawing would be not be required, if Applicant were to replace the instant Sequence Listing with a substitute Sequence Listing that include the sequences depicted in Figure 12, and then amend the brief description of the figure at page 18 of the specification to include a reference to the sequence identification number identifying the sequence as it is listed. Alternatively, Applicant could remedy this issue, so that a replacement drawing would be not be required, by amending the brief description of the figure at page 18 of the specification to recite that the sequences depicted in the figure are the sequences of amino acids 1-55 and 57-553 of SEQ ID NO: 8.

New Grounds of Rejection

14. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description'' Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

Claim 10 is directed to a method for detecting the presence of anti-CV2 antibodies in a biological sample, said method comprising contacting a biological sample with a purified polypeptide comprising SEQ ID NO: 8, or a fragment thereof that binds to anti-CV2 antibodies, or with "a polypeptide encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7".

Accordingly, claim 10 is directed to a genus of polypeptides that includes a polypeptide comprising SEQ ID NO: 8, a fragment of a polypeptide comprising SEQ ID NO: 8 that binds to anti-CV2 antibodies, and any other "polypeptide encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7".

The polypeptide encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7 is not necessarily a polypeptide comprising SEQ ID NO: 8, nor is it necessarily a fragment of a polypeptide comprising SEQ ID NO: 8 that binds to anti-CV2 antibodies.

In fact, giving the claim the broadest, reasonable interpretation that is consistent with the specification and that which would be understood by the skilled artisan, a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7 encodes a plurality of different proteins, only some of which are encoded by the same open reading frame as that which encodes the amino acid sequence of SEQ ID NO: 8. Moreover, some of these polypeptides may have amino acid sequences that are fragments of SEQ ID NO: 8, but which do not contain the antigenic determinants to which anti-CV2 antibodies bind. Thus, claim 10 is directed to a genus of polypeptides, which although encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7, vary substantially in structure and function.

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) states, "[p]ossession

may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). "Guidelines" further states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claim encompasses a genus of variant species of polypeptide that are encoded by the nucleotide sequence of SEQ ID NO: 7, but which can otherwise have substantially different structures and functions, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

15. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a method for detecting the presence of anti-CV2 antibodies in a biological sample, said method comprising contacting a biological sample with a purified polypeptide comprising SEQ ID NO: 8, or a fragment thereof that binds to anti-CV2 antibodies, **does not reasonably provide enablement for using** a method for detecting the presence of anti-CV2 antibodies in a biological sample, said method comprising contacting a biological sample with any polypeptide encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 10 is directed to a method for detecting the presence of anti-CV2 antibodies in a biological sample, said method comprising contacting a biological sample with a purified polypeptide comprising SEQ ID NO: 8, or a fragment thereof that binds to anti-CV2 antibodies, or with "a polypeptide encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7".

Accordingly, claim 10 is directed to a genus of polypeptides that includes a polypeptide comprising SEQ ID NO: 8, a fragment of a polypeptide comprising SEQ ID NO: 8 that binds to anti-CV2 antibodies, and any other "polypeptide encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7".

As explained in the "written description" rejection above, the polypeptide encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7 is not necessarily a polypeptide comprising SEQ ID NO: 8, nor is it necessarily a fragment of a polypeptide comprising SEQ ID NO: 8 that binds to anti-CV2 antibodies. In fact, giving the claim the broadest, reasonable interpretation that is consistent with the specification and that which would be understood by the skilled artisan, a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7 encodes a plurality of different proteins, only some of which are encoded by the same open reading frame as that which encodes the amino acid sequence of SEQ ID NO: 8. Moreover, some of these polypeptides may have amino acid sequences that are fragments of SEQ ID NO: 8, but which do not contain the antigenic determinants to which anti-CV2 antibodies bind. Thus, claim 10 is directed to a genus of polypeptides, which although encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7 vary substantially in structure and function.

The specification does not teach a method for detecting the presence of anti-CV2 antibodies in a biological sample, said method comprising contacting a biological sample with "a polypeptide encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 7", which is not also a polypeptide comprising SEQ ID NO: 8 or otherwise a fragment of a polypeptide comprising SEQ ID NO: 8 that binds to anti-CV2 antibodies.

As explained in preceding Office actions, only a polypeptide comprising SEQ ID NO: 8 or a polypeptide comprising a fragment of a polypeptide comprising SEQ ID NO: 8 that binds to anti-CV2 antibodies can be used without undue and/or unreasonable experimentation as a means for detecting the presence of anti-CV2 antibodies in a biological sample.

16. Claim 4 is rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Byk (Database GenEMBL Accession No. Y10976, 09 May 1997) (of record), as evidenced by result 3 of the attached copy of USPTO search report (i.e., "us-09-367-496c-7.rge"), which was generated September 7, 2005 using SEQ ID NO: 7 as a query.

The claim is drawn to an isolated nucleic acid comprising a cDNA sequence coding for a ULIP polypeptide of amino acid sequence SEQ ID NO: 8, wherein said nucleic acid molecule comprises the sequence of SEQ ID NO: 7.

More succinctly, the claim is drawn to an isolated nucleic acid comprising the polynucleotide sequence of SEQ ID NO: 7.

Byk teaches an isolated nucleic acid molecule comprising a polynucleotide sequence that is 99.9% identical to the polynucleotide sequence set forth as SEQ ID NO: 7.

As evidenced by result 3 of the attached copy of USPTO search report (i.e., "us-09-367-496c-7.rge"), which was generated September 7, 2005 using SEQ ID NO: 7 as a query, the disclosed polynucleotide and the polynucleotide sequence set forth as SEQ ID NO: 7 are the same length. The disclosed polynucleotide differs from the polynucleotide sequence of SEQ ID NO: 7 at only one position, namely position 197. At this position of the disclosed sequence there is "N", which symbol denotes any nucleotide residue (i.e., A, C, G, or T).

The original polynucleotide and amino acid sequences deposited by Byk (i.e., GenEMBL Accession Number Y10976) were revised May 10, 1997. The revision history of GenEMBL Accession Number Y10976 may be viewed on the Internet at http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=nucleotide&val=2077995. To view the revision history and determine the changes that were made, select the "Reports" pull-down menu; then select the "Revision History" option.

Given the revision history of the disclosed sequences, it appears that it had been appreciated that the nucleotide at position 197 of the polynucleotide sequence of the isolated nucleic acid molecule is not a T, since if it were there would be a nonsense or "stop" codon placed at that position, which would prematurely terminate translation at that site and before the end of the most probable and longest open-reading frame. However, it appears that it was not known at the time the sequences were revised which other nucleotide (i.e., A, C, or G) is actually found at this position in the polynucleotide sequence of the isolated nucleic acid molecule. Nevertheless, the polynucleotide sequence of a nucleic acid molecule is an inherent feature; furthermore, Byk discloses the isolated nucleic acid encodes a human polypeptide designated "ULIP4". Notably the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed nucleic acid. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed nucleic acid molecule is different than that taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989). Therefore, absent a showing of any factual evidence otherwise, the nucleic acid molecule disclosed by Byk is deemed the same as the claimed nucleic acid molecule.

It is further duly noted that Byk does not teach that the polynucleotide sequence of the disclosed nucleic acid molecule encodes a ULIP polypeptide of amino acid sequence SEQ ID NO: 8. Nevertheless, the claimed nucleic acid molecule encoding a ULIP polypeptide of amino acid sequence SEQ ID NO: 8 is defined by claim 4 as a nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 7, which for the reasons explained in the paragraph above is deemed the same as the claimed nucleic acid molecule.

Although it may not have been appreciated at the time the information was deposited into the database that the amino acid at position 56 of the amino acid sequence of the polypeptide encoded by the isolated nucleic acid molecule is lysine, or that the polypeptide comprises an additional 19 amino acid residues at the carboxy-terminus, just as the polynucleotide sequence of a nucleic acid molecule is an inherent feature, so is the amino acid sequence that it encodes. But for the amino acid residue at position 56, Byk teaches the nucleic acid molecule encodes a

polypeptide comprising amino acids 1-553 of SEQ ID NO: 8, which is, again, a human polypeptide that has been designated "ULIP4". This same nomenclature is used in the specification to identify the polypeptide of SEQ ID NO: 8; see, e.g., page 18, lines 20-22. As such, it appears the nucleic acid molecule disclosed by the prior art, which comprises a polynucleotide sequence that is deemed the same as the polynucleotide sequence of SEQ ID NO: 7, necessarily encodes the same polypeptide (i.e., a polypeptide comprising the amino acid sequence of SEQ ID NO: 8).

If claim 4 is not anticipated under 35 U.S.C. 102(a) Byk (Database GenEMBL Accession No. Y10976, 09 May 1997), the claimed nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 7 would have been *prima facie* obvious given the disclosure by the prior art. Again, given the revision history described above, it would have been obvious to one ordinarily skilled in the art at the time of the invention that the nucleotide at position 197 of the polynucleotide sequence of the isolated nucleic acid molecule is not a T. If it were, there would be a nonsense or "stop" codon placed at that position, which would prematurely terminate translation at that site and before the end of the most probable and longest open-reading frame. This assertion is further supported by the "CDS" (i.e., coding sequence) annotations, which indicate that there had been a mistake in reverse transcription of the nucleotide sequence at the position of the codon comprised of nucleotides 197-199. Because of this mistake, the sequence was revised on May 10, 1997; the original nucleotide sequence was changed so that "N", rather than "T", is listed in the sequence at position 197. Accordingly, although it appears that it was not known at the time the sequences were revised which other nucleotide (i.e., A, C, or G) is actually found at this position in the polynucleotide sequence of the isolated nucleic acid molecule, it would have been obvious to one ordinarily skilled in the art at the time of the invention that the nucleotide is A, C, or G, and given this fact, the claimed nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 7 would have been obvious.

See MPEP § 2144.08; *In re Petering*, 301 F.2d 676, 681, 133 USPQ 275, 280 (CCPA 1962); and *In re Schaumann*, 572 F.2d 312, 316, 197 USPQ 5, 9 (CCPA 1978).

17. Applicant cannot rely upon the foreign priority papers to overcome the above rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
November 16, 2005

Notice to Comply	Application No.	Applicant(s)	
	09/367,496	AGUERA ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The reason the application is deficient is explained in the Office action.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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